

In The Claims

1. (canceled) A method for altering a B cell mediated pathology in a patient, said method comprising:  
 administering a composition comprising a chimeric protein;  
 said chimeric protein comprising at least a portion of a VH or VL region and at least a portion of an immunoglobulin constant region;  
 wherein said VH or VL region is associated with a B cell clone from said patient having said B cell mediated pathology;  
 and said administering of said composition alters said B cell mediated pathology in said patient.

2. (canceled) The method of claim 1 wherein said composition further comprises a second chimeric protein that comprises at least a portion of VH or VL region and at least a portion of a second immunoglobulin constant region.

3. (canceled) The method of claim 1 wherein said immunoglobulin constant region comprises a human IgGg1 constant region.

4. (canceled) The method of claim 1 wherein said VH or VL region is a VH region.

5. (canceled) The method of claim 1 wherein said VH or VL region is a VL region.

6. (canceled) The method of claim 1 or 2 wherein said VH or VL region of said first chimeric protein comprises a VH region and said second chimeric protein comprises a VL region.

7. (canceled) The method of claim 2 wherein said second immunoglobulin constant region comprises a human  $\kappa$  or  $\lambda$  constant region.

8. (canceled) The method of claim 1 or 2 wherein said VH or VL region is an entire variable region.

9. (canceled) The method of claim 1 or 2 wherein said VL region is an entire variable region.

10. (canceled) The method of claim 1 or 2 wherein said first or second immunoglobulin constant region is selected from the group consisting of a human IgGg1 constant region, a human IgGg2 constant region, a human IgGg3 constant region, a human IgGg4 constant region, a human IgA1 constant region, a human IgA2 constant region, a human IgM constant region, a human IgD constant region, a human IgE constant region, a human  $\kappa$  chain constant region, and a human  $\lambda$  chain constant region.

11. (canceled) The method of claim 1 wherein said chimeric protein is produced by a method comprising:  
isolating a gene encoding at least a portion of a VH or VL region from B cells of said patient having said B cell mediated pathology;  
inserting said gene encoding said VH or VL region and a gene encoding at least a portion of said immunoglobulin constant region into an expression vector to allow the expression of said first chimeric protein;  
producing said chimeric protein by introducing said expression vector into insect cell lines; and  
isolating said chimeric protein.
12. (canceled) The method of claim 11 further comprising the step of inserting a gene encoding at least a portion of a VH or VL region and a gene encoding at least a portion of a second immunoglobulin constant region into said expression vector to allow the expression of said second chimeric protein.
13. (canceled) The method of claim 11 or 12 further comprises a step of conjugating said chimeric protein to a carrier protein.
14. (canceled) The method of claim 13 wherein said carrier protein is keyhole-limpet hemocyanin (KLH).
15. (canceled) The method of claim 1 wherein said composition is further co-administered with a cytokine or chemokine.
16. (canceled) The method of claim 15 wherein said cytokine is granulocyte-macrophage-colony stimulating factor (GM-CSF).
17. (withdrawn) The method of claim 15 wherein said chemokine is monocyte chemotactic protein 3 (MCP 3).
18. (canceled) The method of claim 11 wherein said expression vector is a baculovirus expression vector.
19. (canceled) The method of claim 18 wherein said baculovirus expression vector comprises a honey bee melittin secretory signal sequence and a human placental alkaline phosphatase secretory signal sequence.
20. (canceled) The method of claim 19 wherein said baculovirus expression vector further comprises a baculovirus AcNPV p10 promotor and AcNPV polyhedrin promotor, wherein said p10 promotor controls a honey bee melittin secretory signal sequence, and wherein

said polyhedrin promotor controls a human placental alkaline phosphatase secretory signal sequence.

21. (canceled) The method of claim 20 wherein a gene encoding a chimeric protein comprising a VH region and a first immunoglobulin constant region is controlled by said p10 promotor in said baculovirus expression vector, a gene encoding a chimeric protein comprising a VL region and a second first immunoglobulin constant region is controlled by polyhedrin promotor in said baculovirus expression vector.

22. (canceled) The method of claim 20 wherein said gene comprising said VH or VL region and said gene encoding said immunoglobulin constant region is controlled by either said p10 promotor or polyhedrin promotor in said baculovirus expression vector.

23. (canceled) The method of claim 11 wherein said gene encoding said immunoglobulin constant region is a human IgGg1 gene.

24 (canceled) The method of claim 12 wherein said gene encoding said second immunoglobulin constant region is a gene encoding for a human  $\kappa$  or  $\lambda$  constant region.

25. (canceled) The method of claim 11 or 12 wherein said gene encoding said immunoglobulin constant region is selected from the group consisting of a human IgGg1 constant region, a human IgGg2 constant region, a human IgGg3 constant region, a human IgGg4 constant region, a human IgA1 constant region, a human IgA2 constant region, a human IgM constant region, a human IgD constant region, a human IgE constant region, a human k chain constant region, and a human l chain constant region.

26. (canceled) The method of claim 11 wherein said chimeric protein is selected from the group consisting of a protein comprising said VH region and a human IgGg1 constant region; a protein comprising said VL region and a human k chain constant region; and a protein comprising said VL region and a human l chain constant region.

27. (canceled) The method of claim 12 wherein said first and second chimeric proteins comprise a protein comprising said VH region and a human IgGg1 constant region and a protein comprising said VL region and a human k or l chain constant region.

28. (canceled) The method of claim 11 wherein said insect cell lines are Trichoplusia ni (Hi – 5) or Spodoptera frugiperda (sf9) cell lines.

29. (canceled) The method of claim 11 or 12 wherein said chimeric proteins are analyzed for expression by ELISA.

30. (canceled) The method of claim 11 or 12 wherein said chimeric proteins are isolated using a protein selected from the group consisting of protein A, protein G, protein L and other proteins being able to bind to an immunoglobulin binding domain.

31. (canceled) The method of claim 30 wherein said other protein able to bind an immunoglobulin binding domain is an anti-immunoglobulin antibody.

32. (canceled) The method of claim 1 wherein said B cell mediated pathology is a B cell lymphoma.

33. (canceled) The method of claim 32 wherein said B cell lymphoma is refractory low grade lymphoma or follicular B cell lymphoma.

34. (withdrawn) A composition for altering a B cell mediated pathology in a patient comprising:  
a chimeric protein that comprises at least a portion of a VH or VL region linked to at least a portion of an immunoglobulin constant region, wherein said VH or VL region is associated with a B cell clone from said patient having said B cell mediated pathology.

35. (withdrawn) A composition of claim 34 further comprising a second chimeric protein that comprises at least a portion of a variable region of a VH or VL region and at least a portion of a second immunoglobulin constant region, wherein said variable region is associated with a B cell clone from said patient having said B cell mediated pathology.

36. (withdrawn) The composition of claim 34 or 35 wherein said chimeric proteins are produced in according to claim 13 or 14.

37. (withdrawn) The composition of claim 34 or 35 wherein said immunoglobulin constant regions are selected from the group consisting of a human IgGg1 constant region, a human IgGg2 constant region, a human IgGg3 constant region, a human IgGg4 constant region, a human IgA1 constant region, a human IgA2 constant region, a human IgM constant region, a human IgD constant region, a human IgE constant region, a human k chain constant region, and a human l chain constant region

38. (withdrawn) The composition of claim 34 wherein said immunoglobulin constant region is a human IgGg1 constant region operatively linked to said VH region.

39. (withdrawn) The composition of claim 34 wherein said immunoglobulin constant region is a human k or l constant region operatively linked to said VL region.

40. (withdrawn) The composition claim 35 wherein said first and second chimeric proteins are said VH region operatively linked to a human IgG1 constant region and said VL region operatively linked to a human k or l constant region.
41. (withdrawn) The composition of claim 34 or 35 further comprises a carrier protein.
42. (withdrawn) The composition of claim 41 wherein said carrier protein is keyhole-limpet hemocyanin (KLH).
43. (withdrawn) The composition of claim 34 or 35 is further co-administered with a cytokine or chemokine.
44. (withdrawn) The composition of claim 43 wherein said cytokine is granulocyte-macrophage-CSF.
45. (withdrawn) The composition of claim 43 wherein said chemokine is a monocyte chemotactic protein 3 (MCP 3).
46. (withdrawn) The composition of claim 34 or 35 wherein said composition is a vaccine.
47. (withdrawn) The composition of claim 34 wherein said B cell mediated pathology is a B cell lymphoma.
48. (withdrawn) The composition of claim 47 wherein said B cell lymphoma is non-Hodgkins lymphoma.
49. (withdrawn) The composition of claim 47 wherein said B cell lymphoma is refractory low grade or follicular B cell lymphoma.
50. (withdrawn) The composition of claim 34 is further administered by injection, inhalation, oral or transdermal delivery.
51. (withdrawn) The composition of claim 34 wherein said B cell mediated pathology is an autoimmune disease selected from the group consisting of multiple sclerosis, systemic lupus erythematosus, anti-Hu associated paraneoplastic neurological syndrome, autoimmune hepatitis, Type I diabetes, autoimmune thyroiditis, and scleroderma.
52. (withdrawn) An expression vector comprising (a) a chimeric gene encoding a portion of a VL region and a portion of a gene encoding a k light chain, both operatively linked to a human placental alkaline phosphatase secretory signal sequence and a polyhedrin promoter, and (b) a chimeric gene encoding a portion of a VH region and a portion of an IgG1 heavy chain, both operatively linked to a honey bee melittin secretory signal sequence and a P10 promoter.

53. (withdrawn) A baculovirus expression vector comprising (a) a chimeric gene encoding a portion of a VL region and a portion of a gene encoding a l light chain, both operatively linked to a human placental alkaline phosphatase secretory signal sequence and a polyhedrin promoter, and (b) a chimeric gene encoding a portion of a VH region and a portion of an IgG1 heavy chain, both operatively linked to a honey bee melittin secretory signal sequence and a P10 promoter.

54. (withdrawn) An expression vector comprising (a) a portion of a gene encoding a k light chain constant region operatively linked to a human placental alkaline phosphatase secretory signal sequence and a polyhedrin promoter, and (b) a portion of a gene encoding an IgG1 heavy chain constant region operatively linked to a honey bee melittin secretory signal sequence and a P10 promoter.

55. (withdrawn) An expression vector comprising (a) a portion of a gene encoding a l light chain constant region operatively linked to a human placental alkaline phosphatase secretory signal sequence and a polyhedrin promoter, and (b) a portion of a gene encoding an IgG1 heavy chain constant region operatively linked to a honey bee melittin secretory signal sequence and a P10 promoter.

56. (withdrawn) A vector comprising the nucleic acid sequence as set forth in SEQ ID NO:6.

57. (withdrawn) A vector comprising the nucleic acid sequence as set forth in SEQ ID NO:7.

58. (withdrawn) A vector comprising the nucleic acid sequence as set forth in SEQ ID NO:89.

59. (withdrawn) A vector comprising the nucleic acid sequence as set forth in SEQ ID NO:90.

60. (withdrawn) A vector comprising the nucleic acid sequence as set forth in SEQ ID NO:91.

61. (new) A method for altering a B cell mediated malignancy in a patient, said method comprising:

administering a composition comprising two chimeric proteins; wherein

(1) the first chimeric protein comprises at least a portion of a V<sub>H</sub> region and at least a portion of an immunoglobulin constant region,

(2) the second chimeric protein comprises at least a portion of a V<sub>L</sub> region and at

least a portion of an immunoglobulin constant region, and  
 (3) wherein said V<sub>H</sub> and said V<sub>L</sub> region are associated with a B cell clone from said patient having said B cell mediated malignancy,  
 wherein said chimeric proteins are produced in insect cells; and  
 said administering of said composition alters said B cell mediated malignancy in said patient.

62. (new) The method of claim 61 wherein said V<sub>H</sub> or V<sub>L</sub> region is an entire variable region.

63. (new) The method of claim 61 wherein said second chimeric protein comprises an immunoglobulin constant region comprising a human kappa or lambda constant region.

64. (new) The method of claim 61 wherein said first chimeric protein comprises an immunoglobulin constant region is selected from the group consisting of a human IgG<sub>γ1</sub> constant region, a human IgG<sub>γ2</sub> constant region, a human IgG<sub>γ3</sub> constant region, a human IgG<sub>γ4</sub> constant region, a human IgA<sub>1</sub> constant region, a human IgA<sub>2</sub> constant region, a human IgM constant region, a human IgD constant region, and a human IgE constant region.

65. (new) The method of claim 64 wherein said first chimeric protein comprises an immunoglobulin constant region comprising a human IgG<sub>γ1</sub> constant region.

66. (new) The method of claim 61 further comprising a step of conjugating said chimeric proteins to a carrier protein.

67. (new) The method of claim 66 wherein said carrier protein is keyhole-limpet hemocyanin (KLH).

68. (new) The method of claim 61 wherein said composition is further co-administered with a cytokine or chemokine.

69. (new) The method of claim 68 wherein said cytokine is granulocyte-macrophage-colony stimulating factor (GM-CSF).

70. (new) The method of claim 61 wherein said chimeric protein is produced by a method comprising:

isolating a gene encoding at least a portion of a V<sub>H</sub> region and at least a portion of a V<sub>L</sub> region from B cells of said patient having said B cell mediated pathology;  
 inserting said gene encoding said V<sub>H</sub> region into an expression vector comprising a portion of an immunoglobulin constant region to allow the expression of said first chimeric protein; and

inserting said gene encoding said V<sub>L</sub> region into an expression vector comprising a portion of an immunoglobulin constant region to allow the expression of said second chimeric protein;  
 producing said chimeric protein by introducing said expression vector into insect cell lines; and  
 isolating said chimeric protein.

71. (new) The method of claim 70 wherein said expression vector is a baculovirus expression vector.

72. (new) The method of claim 71 wherein said baculovirus expression vector comprises a honey bee melittin secretory signal sequence and a human placental alkaline phosphatase secretory signal sequence.

73. (new) The method of claim 72 wherein said baculovirus expression vector further comprises a baculovirus AcNPV p10 promotor and AcNPV polyhedrin promotor, wherein said p10 promotor controls a honey bee melittin secretory signal sequence, and wherein said polyhedrin promotor controls a human placental alkaline phosphatase secretory signal sequence.

74. (new) The method of claim 73 wherein a gene encoding a chimeric protein comprising a V<sub>L</sub> region and a second immunoglobulin constant region is controlled by polyhedrin promotor in said baculovirus expression vector, and a gene encoding a chimeric protein comprising a V<sub>H</sub> region and a first immunoglobulin constant region is controlled by said p10 promotor in said baculovirus expression vector.

75. (new) The method of claim 70 wherein said gene comprising said V<sub>H</sub> or V<sub>L</sub> region and said gene encoding said immunoglobulin constant region is controlled by either said p10 promotor or polyhedrin promotor in said baculovirus expression vector.

76. (new) The method of claim 61 wherein said first and second chimeric proteins comprise a protein comprising said V<sub>H</sub> region and a human IgGγ<sub>1</sub> constant region and a protein comprising said V<sub>L</sub> region and a human kappa or lambda chain constant region.

77. (new) The method of claim 61 wherein said insect cell lines are *Trichoplusia ni* or *Spodoptera frugiperda* (Sf9) cell lines.

78. (new) The method of claim 61 wherein said chimeric proteins are analyzed for expression by ELISA.



79. (new) The method of claim 61 wherein said chimeric proteins are isolated using a protein selected from the group consisting of protein A, protein G, protein L and other proteins being able to bind to an immunoglobulin binding domain.

80. (new) The method of claim 79 wherein said other protein able to bind an immunoglobulin binding domain is an anti-immunoglobulin antibody.

81. (new) The method of claim 61 wherein said B cell mediated malignancy is a B cell lymphoma.

82. (new) The method of claim 80 wherein said B cell lymphoma is refractory low grade lymphoma or follicular B cell lymphoma.